

Appl. No. : 10/623,119  
Filed : July 17, 2003

AMENDMENTS TO THE SPECIFICATION

Please amend the first paragraph of the specification, page 1, lines 3-4, as follows:

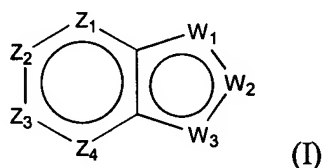
~~This application claims the benefit of priority of copending U.S. Provisional Application Serial Number 60/200,791, filed April 28, 2000.~~

This application is a divisional of U.S. Patent Application Serial No. 09/844,685, entitled "MUSCARINIC AGONISTS," filed April 27, 2001, now U.S. Patent No. 6,627,645, issued September 30, 2003, by Andersson, et al., which in turn claims priority to U.S. Provisional Patent Application Serial No. 60/200,791, filed April 28, 2000, all of which are incorporated by reference herein in their entirety, including any drawings.

AMENDMENTS TO THE CLAIMS

Please amend the claims as follows:

1. (CURRENTLY AMENDED) A compound of formula (I):

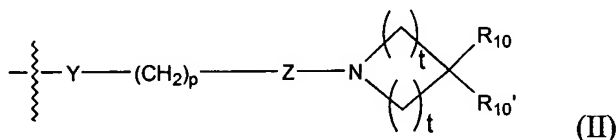


wherein:

~~Z<sub>1</sub> is CR<sub>1</sub> or N, Z<sub>2</sub> is CR<sub>2</sub> or N, Z<sub>3</sub> is CR<sub>3</sub> or N, and Z<sub>4</sub> is CR<sub>4</sub> or N, where no more than two of Z<sub>1</sub>, Z<sub>2</sub>, Z<sub>3</sub> and Z<sub>4</sub> are N;~~

~~W<sub>1</sub> is O, or S, or NR<sub>5</sub>; one of W<sub>2</sub> and W<sub>3</sub> is N or CR<sub>6</sub>, and the other of W<sub>2</sub> and W<sub>3</sub> is CG; W<sub>1</sub> is NG, W<sub>2</sub> is CR<sub>5</sub> or N, and W<sub>3</sub> is CR<sub>6</sub> or N; or W<sub>1</sub> and W<sub>3</sub> are N, and W<sub>2</sub> is NG;~~

G is of formula (II):



Y is O, S, CHOH, -NHC(O)-, -C(O)NH-, -C(O)-, -OC(O)-, -(O)CO-, -NR<sub>7</sub>-, -CH=N-, or absent;

p is 1, 2, 3, 4 or 5;

Z is CR<sub>8</sub>R<sub>9</sub> or absent;

each t is 1, 2, or 3;

each R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, and R<sub>4</sub>, independently, is H, amino, hydroxyl, halo, or straight- or branched-chain C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> heteroalkyl, C<sub>1-6</sub> haloalkyl, -CN, -CF<sub>3</sub>, -OR<sub>11</sub>, -COR<sub>11</sub>, -NO<sub>2</sub>, -SR<sub>11</sub>, -NHC(O)R<sub>11</sub>, -C(O)NR<sub>12</sub>R<sub>13</sub>, -NR<sub>12</sub>R<sub>13</sub>, -NR<sub>11</sub>C(O)NR<sub>12</sub>R<sub>13</sub>, -SO<sub>2</sub>NR<sub>12</sub>R<sub>13</sub>, -OC(O)R<sub>11</sub>, -O(CH<sub>2</sub>)<sub>q</sub>NR<sub>12</sub>R<sub>13</sub>, or -(CH<sub>2</sub>)<sub>q</sub>NR<sub>12</sub>R<sub>13</sub>, where q is an integer from 2 to 6, or R<sub>1</sub> and R<sub>2</sub> together form -NH-N=N- or R<sub>3</sub> and R<sub>4</sub> together form -NH-N=N-;

each R<sub>5</sub>, R<sub>6</sub>, and R<sub>7</sub>, independently, is H, C<sub>1-6</sub> alkyl; formyl; C<sub>3-6</sub> cycloalkyl; C<sub>5-6</sub> aryl, optionally substituted with halo or C<sub>1-6</sub> alkyl; or C<sub>5-6</sub> heteroaryl, optionally substituted with halo or C<sub>1-6</sub> alkyl;

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each R<sub>8</sub> and R<sub>9</sub>, independently, is H or straight- or branched-chain C<sub>1-8</sub> alkyl;

R<sub>10</sub> is H, straight- or branched-chain C<sub>1-8</sub> alkyl, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, C<sub>1-8</sub> alkylidene, C<sub>1-8</sub> alkoxy, C<sub>1-8</sub> heteroalkyl, C<sub>1-8</sub> aminoalkyl, C<sub>1-8</sub> haloalkyl, C<sub>1-8</sub> alkoxycarbonyl, C<sub>1-8</sub> hydroxyalkoxy, C<sub>1-8</sub> hydroxyalkyl, -SH, C<sub>1-8</sub> alkylthio, -O-CH<sub>2</sub>-C<sub>5-6</sub> aryl, -C(O)-C<sub>5-6</sub> aryl substituted with C<sub>1-3</sub> alkyl or halo, C<sub>5-6</sub> aryl, C<sub>5-6</sub> cycloalkyl, C<sub>5-6</sub> heteroaryl, C<sub>5-6</sub> heterocycloalkyl, -NR<sub>12</sub>R<sub>13</sub>, -C(O)NR<sub>12</sub>R<sub>13</sub>, -NR<sub>11</sub>C(O)NR<sub>12</sub>R<sub>13</sub>, -CR<sub>11</sub>R<sub>12</sub>R<sub>13</sub>, -OC(O)R<sub>11</sub>, -(O)(CH<sub>2</sub>)<sub>s</sub>NR<sub>12</sub>R<sub>13</sub> or -(CH<sub>2</sub>)<sub>s</sub>NR<sub>12</sub>R<sub>13</sub>, s being an integer from 2 to 8;

R<sub>10'</sub> is H, straight- or branched-chain C<sub>1-8</sub> alkyl, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, C<sub>1-8</sub> alkylidene, C<sub>1-8</sub> alkoxy, C<sub>1-8</sub> heteroalkyl, C<sub>1-8</sub> aminoalkyl, C<sub>1-8</sub> haloalkyl, C<sub>1-8</sub> alkoxycarbonyl, C<sub>1-8</sub> hydroxyalkoxy, C<sub>1-8</sub> hydroxyalkyl, or C<sub>1-8</sub> alkylthio;

each R<sub>11</sub>, independently, is H, straight- or branched-chain C<sub>1-8</sub> alkyl, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, C<sub>2-8</sub> heteroalkyl, C<sub>2-8</sub> aminoalkyl, C<sub>2-8</sub> haloalkyl, C<sub>1-8</sub> alkoxycarbonyl, C<sub>2-8</sub> hydroxyalkyl, -C(O)-C<sub>5-6</sub> aryl substituted with C<sub>1-3</sub> alkyl or halo, C<sub>5-6</sub> aryl, C<sub>5-6</sub> heteroaryl, C<sub>5-6</sub> cycloalkyl, C<sub>5-6</sub> heterocycloalkyl, -C(O)NR<sub>12</sub>R<sub>13</sub>, -CR<sub>5</sub>R<sub>12</sub>R<sub>13</sub>, -(CH<sub>2</sub>)<sub>t</sub>NR<sub>12</sub>R<sub>13</sub>, t is an integer from 2 to 8; and

each R<sub>12</sub> and R<sub>13</sub>, independently, is H, C<sub>1-6</sub> alkyl; C<sub>3-6</sub> cycloalkyl; C<sub>5-6</sub> aryl, optionally substituted with halo or C<sub>1-6</sub> alkyl; or C<sub>5-6</sub> heteroaryl, optionally substituted with halo or C<sub>1-6</sub> alkyl; or R<sub>12</sub> and R<sub>13</sub> together form a cyclic structure;

or a pharmaceutically acceptable salt, ester or prodrug thereof.

2. (ORIGINAL) The compound of claim 1, wherein each t is 2 and R<sub>10</sub> is straight- or branched-chain C<sub>2-8</sub> alkyl, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, C<sub>1-8</sub> alkylidene, C<sub>1-8</sub> alkoxy, or C<sub>1-8</sub> heteroalkyl.

3. (ORIGINAL) The compound of claim 2, wherein R<sub>10</sub> is n-butyl.

4. (CANCELED)

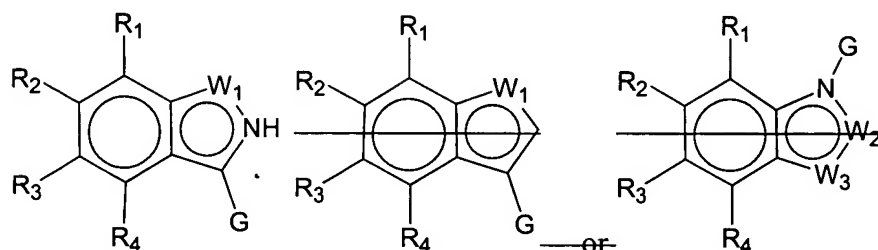
5. (CURRENTLY AMENDED) The compound of claim 4, wherein each R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, and R<sub>4</sub>, independently, is H, hydroxyl, halo, C<sub>1-6</sub>heteroalkyl, CF<sub>3</sub>, -NO<sub>2</sub>, or straight- or branched-chain C<sub>1-6</sub> alkyl, or R<sub>1</sub> and R<sub>2</sub> together form -NH-N=N- or R<sub>3</sub> and R<sub>4</sub> together form -NH-N=N-.

6. (ORIGINAL) The compound of claim 2, wherein Y is absent or O, p is 0, 1, 2 or 3, and R<sub>8</sub> and R<sub>9</sub> are H.

7. (ORIGINAL) The compound of claim 6, wherein Z is absent, Y is absent and p is 3.

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8. (ORIGINAL) The compound of claim 7, wherein R<sub>10</sub> is n-butyl.  
 9. (ORIGINAL) The compound of claim 2, wherein the compound is of the formula



wherein W<sub>1</sub> is O, or S, or NR<sub>5</sub>, W<sub>2</sub> is CR<sub>5</sub> or N, and W<sub>3</sub> is CR<sub>5</sub> or N.

10. (ORIGINAL) The compound of claim 9, wherein Z is absent, Y is absent and p is 3.  
 11. (ORIGINAL) The compound of claim 10, wherein R<sub>10</sub> is n-butyl.  
 12. (ORIGINAL) The compound of claim 9, wherein R<sub>5</sub> is H or C<sub>1-6</sub> alkyl.  
 13 - 16. (CANCELED)  
 17. (CURRENTLY AMENDED) The compound of claim 1, wherein the compound is:

~~2-(3-(4-n-butylpiperidin-1-yl)propyl)-benzothiazole;~~  
~~2-(3-(4-n-butylpiperidin-1-yl)propyl)-benzooxazole;~~  
~~4,5-difluoro-2-(3-(4-n-butylpiperidin-1-yl)propyl)-1H-benzoimidazole;~~  
~~6-fluoro-5-nitro-2-(3-(4-n-butylpiperidin-1-yl)propyl)-1H-benzoimidazole;~~  
~~5-tert-butyl-2-(3-(4-n-butylpiperidin-1-yl)propyl)-1H-benzoimidazole;~~  
~~5-chloro-6-methyl-2-(3-(4-n-butylpiperidin-1-yl)propyl)-1H-benzoimidazole;~~  
~~4,6-difluoro-2-(3-(4-n-butylpiperidin-1-yl)propyl)-1H-benzoimidazole;~~  
~~2-(3-(4-n-butylpiperidin-1-yl)propyl)-1H-imidazo[4,5-c]pyridine;~~  
~~8-(3-(4-n-butylpiperidin-1-yl)propyl)-9H-purine;~~  
~~7-(3-(4-n-butylpiperidin-1-yl)propyl)-3,8-dihydro-imidazo[4',5':3,4]benzo[1,2-d][1,2,3]triazole;~~  
~~2-(3-(4-n-butylpiperidin-1-yl)propyl)-3a,4,5,6,7,7a-hexahydro-1H-benzoimidazole;~~  
~~1-(3-(4-n-butylpiperidin-1-yl)propyl)-1H-indole;~~  
~~1-(3-(4-n-butylpiperidin-1-yl)propyl)-1H-benzoimidazole;~~

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~~3-methyl-1-(3-(4-n-butylpiperidine)-1-yl-propyl)-1H-indole;~~  
~~5-bromo-1-(3-(4-n-butylpiperidine)-1-yl-propyl)-1H-indole;~~  
~~3-formyl-1-(3-(4-n-butylpiperidine)-1-yl-propyl)-1H-indole;~~  
~~7-bromo-1-(3-(4-n-butylpiperidine)-1-yl-propyl)-1H-indole;~~  
~~1-(3-(4-n-butylpiperidine)-1-yl-propyl)-1H-indazole;~~  
~~3-(3-(4-n-butylpiperidine)-1-yl-propyl)-benzo[d]isoxazole;~~  
~~3-(3-(4-n-butylpiperidine)-1-yl-propyl)-1H-indole;~~  
~~4-nitro-2-(3-(4-n-butylpiperidine)-1-yl-propyl)-1H-benzoimidazole;~~  
~~5-nitro-2-(3-(4-n-butylpiperidine)-1-yl-propyl)-1H-benzoimidazole;~~  
~~4-hydroxy-2-(3-(4-n-butylpiperidine)-1-yl-propyl)-1H-benzoimidazole;~~  
~~2-(3-(4-n-butylpiperidine)-1-yl-propyl)-1H-benzoimidazole;~~  
~~4-methyl-2-(3-(4-n-butylpiperidine)-1-yl-propyl)-1H-benzoimidazole;~~  
~~3-(2-(4-n-butylpiperidine)-1-yl-ethyl)-1H-indole;~~  
~~3-(3-(4-n-butylpiperidine)-1-yl-propyl)-1H-indazole;~~  
~~3-(2-(4-n-butylpiperidine)-ethoxy)-7-methyl-benzo[d]isoxazole;~~  
~~1-(3-(4-Methylpiperidine)-1-yl-propyl)-1H-indazole;~~  
~~1-(3-(4-Pentylpiperidine)-1-yl-propyl)-1H-indazole;~~  
~~1-(3-(4-Propylpiperidine)-1-yl-propyl)-1H-;~~  
~~1-(3-(4-(3-Methyl-butyl)-piperidine)-1-yl-propyl)-1H-indazole~~  
~~1-(3-(4-Pentylidene-piperidine)-1-yl-propyl)-1H-indazole;~~  
~~1-(3-(4-Propylidene-piperidine)-1-yl-propyl)-1H-indazole~~  
~~1-Benzo[b]thiophen-2-yl-4-(4-butylpiperidin-1-yl)-butan-1-one~~  
~~4-(4-Butylpiperidin-1-yl)-1-(3-methyl-benzofuran-2-yl)-butan-1-one;~~  
~~4-(4-Butylpiperidin-1-yl)-1-(5-fluoro-3-methyl-benzo[b]thiophen-2-yl)-butan-1-one;~~  
~~1-Benzofuran-2-yl-4-(4-butylpiperidin-1-yl)-butan-1-one;~~  
~~1-(3-Bromo-benzo[b]thiophen-2-yl)-4-(4-butylpiperidin-1-yl)-butan-1-one~~  
~~1-(3-Benzo[b]thiophen-2-yl-propyl)-4-butylpiperidine;~~  
~~1-(3-Benzofuran-2-yl-propyl)-4-butylpiperidine;~~  
~~4-Butyl-1-[3-(3-methyl-benzofuran-2-yl)-propyl]-piperidine;~~  
~~4-Butyl-1-[3-(5-fluoro-3-methyl-benzo[b]thiophen-2-yl)-propyl]-piperidine;~~  
~~2-(3-Iodo-propyl)-benzo[b]thiophene;~~

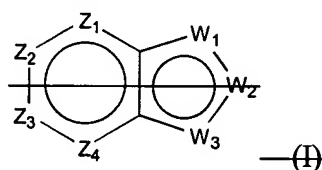
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~~1-(3-Benzo[b]thiophen-2-yl-propyl)-4-methylpiperidine~~  
~~1-(3-Benzo[b]thiophen-2-yl-propyl)-4-benzylpiperidine;~~  
~~1-(3-Benzo[b]thiophen-2-yl-propyl)-4-(2-methoxy-phenyl)-piperidine;~~  
~~2-(3-Bromopropyl)-2H-benzotriazole;~~  
~~2-[3-(4-Butylpiperidin-1-yl)-propyl]-2H-benzotriazole;~~  
~~1-(3-Bromopropyl)-1H-benzotriazole;~~  
~~1-[3-(4-Butylpiperidin-1-yl)-propyl]-1H-benzotriazole;~~  
~~1-[3-(4-Butylpiperidin-1-yl)-propyl]-1H-indole-3-carbaldehyde;~~  
~~{1-[3-(4-Butylpiperidin-1-yl)-propyl]-1H-indol-3-yl}-methanol;~~  
~~1-[3-(4-Butylpiperidin-1-yl)-propyl]-2-phenyl-1H-benzoimidazole;~~  
~~1-[3-(4-Butylpiperidin-1-yl)-propyl]-3-chloro-1H-indazole;~~  
~~1-[3-(4-Butylpiperidin-1-yl)-propyl]-6-nitro-1H-indazole;~~  
~~Benzo[d]isoxazol-3-ol;~~  
~~3-(2-Chloroethoxy)-benzo[d]isoxazole;~~  
~~3-[2-(4-Butylpiperidin-1-yl)-ethoxy]-benzo[d]isoxazol;~~  
~~3-(1H-Indol-3-yl)-propan-1-ol;~~  
~~3-[3-(4-Butyl-piperidin-1-yl)-propyl]-1H-indole hydrochloride;~~  
~~4-(4-Butylpiperidine-1-yl)-butyric acid methyl ester;~~  
~~2-[3-(4-Butylpiperidin-1-yl)-propyl]-1-methyl-1H-benzimidazole;~~  
~~1H-Indazole-3-carboxylic acid (2-(4-butylpiperidin)-1-yl-ethyl)-amide;~~  
~~1-[3-(4-Butylpiperidin-1-yl)-propyl]-5-nitro-1H-indazole;~~  
~~2-[3-(4-butylpiperidin-1-yl)-propyl]-5-nitro-2H-indazole;~~  
~~1-[3-(4-Butyl-piperidin-1-yl)-propyl]-2-methyl-1H-indole;~~  
~~1-{1-[3-(4-Butyl-piperidin-1-yl)-propyl]-1H-indol-3-yl}-ethanone;~~  
~~{1-[3-(4-Butyl-piperidin-1-yl)-propyl]-1H-indol-3-yl}-acetonitrile;~~  
~~1-[3-(4-Butyl-piperidin-1-yl)-propyl]-1H-indole-3-carbonitrile;~~  
~~1-[3-(4-Butyl-piperidin-1-yl)-propyl]-5,6-dimethyl-1H-benzoimidazole;~~  
~~1-[3-(4-Butyl-piperidin-1-yl)-propyl]-5(6)-dimethyl-1H-benzoimidazole;~~  
~~1-[3-(4-Butyl-piperidin-1-yl)-propyl]-5-methoxy-1H-benzoimidazole;~~  
~~{1-[3-(4-Butyl-piperidin-1-yl)-propyl]-1H-benzoimidazol-2-yl}-methanol;~~  
~~1-[3-(4-Butyl-piperidin-1-yl)-propyl]-2-trifluoromethyl-1H-benzoimidazole;~~

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~~(2-Trimethylstannanyl-phenyl)-carbamic acid tert-butyl ester;~~  
~~[2-(4-Chloro-butyryl)-phenyl]-carbamic acid tert-butyl ester;~~  
~~{2-[4-(4-Butyl-piperidine-1-yl)-butyryl]-phenyl}-carbamic acid tert-butyl ester;~~  
~~3-[3-(4-Butyl-piperidine-1-yl)-propyl]-1H-indazole, HCl;~~  
~~3-[3-(4-Butyl-piperidine-1-yl)-propyl]-5-nitro-1H-indazole;~~  
~~3-[3-(4-Butyl-piperidine-1-yl)-propyl]-5,7-dinitro-1H-indazole;~~  
~~4-(4-Butyl-piperidin-1-yl)-1-(2-methylsulfanyl-phenyl)-butan-1-one;~~  
~~or 3-[3-(4-Butyl-piperidin-1-yl)-propyl]-benzo[d]isothiazole;~~  
~~3-[3-(4-Butyl-piperidin-1-yl)-propyl]-5-methoxy-1H-indazole;~~  
~~3-[3-(4-Butyl-piperidin-1-yl)-propyl]-4-methoxy-1H-indazole~~  
~~3-[3-(4-Butyl-piperidin-1-yl)-propyl]-6-methoxy-1H-indazole;~~  
~~3-[3-(4-Butyl-piperidin-1-yl)-propyl]-1H-indazole-4-ol (53MF51);~~  
~~3-[3-(4-Butyl-piperidin-1-yl)-propyl]-1H-indazole-6-ol (53MF52); or~~  
~~3-[3-(4-Butyl-piperidin-1-yl)-propyl]-1H-indazole-5-ol.~~

18. (CURRENTLY AMENDED) A pharmaceutical composition comprising an effective amount of a compound of claim 1 formula (I):

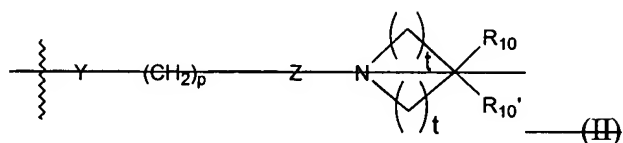


wherein:

~~Z<sub>1</sub> is CR<sub>4</sub> or N, Z<sub>2</sub> is CR<sub>2</sub> or N, Z<sub>3</sub> is CR<sub>3</sub> or N, and Z<sub>4</sub> is CR<sub>4</sub> or N, where no more than two of Z<sub>1</sub>, Z<sub>2</sub>, Z<sub>3</sub> and Z<sub>4</sub> are N;~~

~~W<sub>1</sub> is O, S, or NR<sub>5</sub>, one of W<sub>2</sub> and W<sub>3</sub> is N or CR<sub>6</sub>, and the other of W<sub>2</sub> and W<sub>3</sub> is CG;~~  
~~W<sub>1</sub> is NG, W<sub>2</sub> is CR<sub>5</sub> or N, and W<sub>3</sub> is CR<sub>6</sub> or N; or W<sub>1</sub> and W<sub>3</sub> are N, and W<sub>2</sub> is NG;~~

G is of formula (II):



~~Y is O, S, CHOH, NHC(O), C(O)NH, C(O), OC(O), (O)CO, NR<sub>7</sub>, CH=N, or absent;~~

~~p is 1, 2, 3, 4 or 5;~~

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~~Z is CR<sub>3</sub>R<sub>9</sub> or absent;~~

~~each t is 1, 2, or 3;~~

~~each R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, and R<sub>4</sub>, independently, is H, amino, hydroxyl, halo, or straight or branched chain C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> heteroalkyl, C<sub>1-6</sub> haloalkyl, CN, CF<sub>3</sub>, OR<sub>11</sub>, COR<sub>11</sub>, NO<sub>2</sub>, SR<sub>11</sub>, NHC(O)R<sub>11</sub>, C(O)NR<sub>12</sub>R<sub>13</sub>, NR<sub>12</sub>R<sub>13</sub>, NR<sub>11</sub>C(O)NR<sub>12</sub>R<sub>13</sub>, SO<sub>2</sub>NR<sub>12</sub>R<sub>13</sub>, OC(O)R<sub>11</sub>, O(CH<sub>2</sub>)<sub>q</sub>NR<sub>12</sub>R<sub>13</sub>, or (CH<sub>2</sub>)<sub>q</sub>NR<sub>12</sub>R<sub>13</sub>, where q is an integer from 2 to 6, or R<sub>1</sub> and R<sub>2</sub> together form NH N=N or R<sub>3</sub> and R<sub>4</sub> together form NH N=N;~~

~~each R<sub>5</sub>, R<sub>6</sub>, and R<sub>7</sub>, independently, is H, C<sub>1-6</sub> alkyl, formyl, C<sub>3-6</sub> cycloalkyl, C<sub>5-6</sub> aryl, optionally substituted with halo or C<sub>1-6</sub> alkyl; or C<sub>5-6</sub> heteroaryl, optionally substituted with halo or C<sub>1-6</sub> alkyl;~~

~~each R<sub>8</sub> and R<sub>9</sub>, independently, is H or straight or branched chain C<sub>1-8</sub> alkyl;~~

~~R<sub>10</sub> is straight or branched chain C<sub>1-8</sub> alkyl, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, C<sub>1-8</sub> alkylidene, C<sub>1-8</sub> alkoxy, C<sub>1-8</sub> heteroalkyl, C<sub>1-8</sub> aminoalkyl, C<sub>1-8</sub> haloalkyl, C<sub>1-8</sub> alkoxy carbonyl, C<sub>1-8</sub> hydroxyalkoxy, C<sub>1-8</sub> hydroxyalkyl, SH, C<sub>1-8</sub> alkylthio, O-CH<sub>2</sub>-C<sub>5-6</sub> aryl, C(O)-C<sub>5-6</sub> aryl substituted with C<sub>1-3</sub> alkyl or halo, C<sub>5-6</sub> aryl, C<sub>5-6</sub> cycloalkyl, C<sub>5-6</sub> heteroaryl, C<sub>5-6</sub> heterocycloalkyl, NR<sub>12</sub>R<sub>13</sub>, C(O)NR<sub>12</sub>R<sub>13</sub>, NR<sub>11</sub>C(O)NR<sub>12</sub>R<sub>13</sub>, CR<sub>11</sub>R<sub>12</sub>R<sub>13</sub>, OC(O)R<sub>11</sub>, (O)(CH<sub>2</sub>)<sub>s</sub>NR<sub>12</sub>R<sub>13</sub> or (CH<sub>2</sub>)<sub>s</sub>NR<sub>12</sub>R<sub>13</sub>, s being an integer from 2 to 8;~~

~~R<sub>10'</sub> is H, straight or branched chain C<sub>1-8</sub> alkyl, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, C<sub>1-8</sub> alkylidene, C<sub>1-8</sub> alkoxy, C<sub>1-8</sub> heteroalkyl, C<sub>1-8</sub> aminoalkyl, C<sub>1-8</sub> haloalkyl, C<sub>1-8</sub> alkoxy carbonyl, C<sub>1-8</sub> hydroxyalkoxy, C<sub>1-8</sub> hydroxyalkyl, or C<sub>1-8</sub> alkylthio;~~

~~each R<sub>11</sub>, independently, is H, straight or branched chain C<sub>1-8</sub> alkyl, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, C<sub>2-8</sub> heteroalkyl, C<sub>2-8</sub> aminoalkyl, C<sub>2-8</sub> haloalkyl, C<sub>1-8</sub> alkoxy carbonyl, C<sub>2-8</sub> hydroxyalkyl, C(O)-C<sub>5-6</sub> aryl substituted with C<sub>1-3</sub> alkyl or halo, C<sub>5-6</sub> aryl, C<sub>5-6</sub> heteroaryl, C<sub>5-6</sub> cycloalkyl, C<sub>5-6</sub> heterocycloalkyl, C(O)NR<sub>12</sub>R<sub>13</sub>, CR<sub>5</sub>R<sub>12</sub>R<sub>13</sub>, (CH<sub>2</sub>)<sub>t</sub>NR<sub>12</sub>R<sub>13</sub>, t is an integer from 2 to 8; and~~

~~each R<sub>12</sub> and R<sub>13</sub>, independently, is H, C<sub>1-6</sub> alkyl, C<sub>3-6</sub> cycloalkyl, C<sub>5-6</sub> aryl, optionally substituted with halo or C<sub>1-6</sub> alkyl; or C<sub>5-6</sub> heteroaryl, optionally substituted with halo or C<sub>1-6</sub> alkyl; or R<sub>12</sub> and R<sub>13</sub> together form a cyclic structure;~~

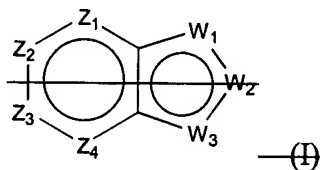
~~or a pharmaceutically acceptable salt, ester or prodrug thereof.~~

19 -34. (CANCELED)



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35. (CURRENTLY AMENDED) A method of increasing an activity of a cholinergic receptor comprising contacting the cholinergic receptor or a system containing the cholinergic receptor with an effective amount of at least one compound of claim 1, formula (I):

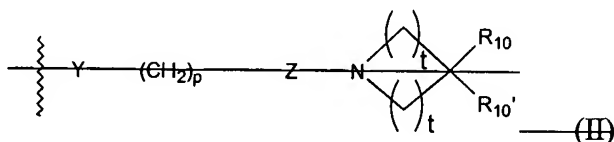


wherein:

Z<sub>1</sub> is CR<sub>1</sub> or N, Z<sub>2</sub> is CR<sub>2</sub> or N, Z<sub>3</sub> is CR<sub>3</sub> or N, and Z<sub>4</sub> is CR<sub>4</sub> or N, where no more than two of Z<sub>1</sub>, Z<sub>2</sub>, Z<sub>3</sub> and Z<sub>4</sub> are N;

W<sub>1</sub> is O, S, or NR<sub>5</sub>, one of W<sub>2</sub> and W<sub>3</sub> is N or CR<sub>6</sub>, and the other of W<sub>2</sub> and W<sub>3</sub> is CG;  
 W<sub>1</sub> is NG, W<sub>2</sub> is CR<sub>5</sub> or N, and W<sub>3</sub> is CR<sub>6</sub> or N; or W<sub>1</sub> and W<sub>3</sub> are N, and W<sub>2</sub> is NG;

G is of formula (II):



Y is O, S, CHOH, NHC(O), C(O)NH, C(O), OC(O), (O)CO, NR<sub>7</sub>, CH=N, or absent;

p is 1, 2, 3, 4 or 5;

Z is CR<sub>8</sub>R<sub>9</sub> or absent;

each t is 1, 2, or 3;

each R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, and R<sub>4</sub>, independently, is H, amino, hydroxyl, halo, or straight or branched chain C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> heteroalkyl, C<sub>1-6</sub> haloalkyl, CN, CF<sub>3</sub>, OR<sub>11</sub>, COR<sub>11</sub>, NO<sub>2</sub>, SR<sub>11</sub>, NHC(O)R<sub>11</sub>, C(O)NR<sub>12</sub>R<sub>13</sub>, NR<sub>12</sub>R<sub>13</sub>, NR<sub>11</sub>C(O)NR<sub>12</sub>R<sub>13</sub>, SO<sub>2</sub>NR<sub>12</sub>R<sub>13</sub>, OC(O)R<sub>11</sub>, O(CH<sub>2</sub>)<sub>q</sub>NR<sub>12</sub>R<sub>13</sub>, or (CH<sub>2</sub>)<sub>q</sub>NR<sub>12</sub>R<sub>13</sub>, where q is an integer from 2 to 6, or R<sub>1</sub> and R<sub>2</sub> together form NHN=N or R<sub>3</sub> and R<sub>4</sub> together form NHN=N;

each R<sub>5</sub>, R<sub>6</sub>, and R<sub>7</sub>, independently, is H, C<sub>1-6</sub> alkyl; formyl; C<sub>2-6</sub> cycloalkyl; C<sub>5-6</sub> aryl, optionally substituted with halo or C<sub>1-6</sub> alkyl; or C<sub>5-6</sub> heteroaryl, optionally substituted with halo or C<sub>1-6</sub> alkyl;

each R<sub>8</sub> and R<sub>9</sub>, independently, is H or straight or branched chain C<sub>1-8</sub> alkyl;

R<sub>10</sub> is straight or branched chain C<sub>1-8</sub> alkyl, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, C<sub>1-8</sub> alkylidene, C<sub>1-8</sub> alkoxy, C<sub>1-8</sub> heteroalkyl, C<sub>1-8</sub> aminoalkyl, C<sub>1-8</sub> haloalkyl, C<sub>1-8</sub> alkoxycarbonyl, C<sub>1-8</sub>

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~~hydroxyalkoxy, C<sub>1-8</sub>-hydroxyalkyl, SH, C<sub>1-8</sub>-alkylthio, O-CH<sub>2</sub>-C<sub>5-6</sub>-aryl, C(O)-C<sub>5-6</sub>-aryl substituted with C<sub>1-3</sub>-alkyl or halo, C<sub>5-6</sub>-aryl, C<sub>5-6</sub>-cycloalkyl, C<sub>5-6</sub>-heteroaryl, C<sub>5-6</sub>-heterocycloalkyl, NR<sub>12</sub>R<sub>13</sub>, C(O)NR<sub>12</sub>R<sub>13</sub>, NR<sub>11</sub>C(O)NR<sub>12</sub>R<sub>13</sub>, CR<sub>11</sub>R<sub>12</sub>R<sub>13</sub>, OC(O)R<sub>11</sub>, (O)(CH<sub>2</sub>)<sub>s</sub>NR<sub>12</sub>R<sub>13</sub> or (CH<sub>2</sub>)<sub>s</sub>NR<sub>12</sub>R<sub>13</sub>, s being an integer from 2 to 8;~~

~~R<sub>10</sub>' is H, straight or branched chain C<sub>1-8</sub>-alkyl, C<sub>2-8</sub>-alkenyl, C<sub>2-8</sub>-alkynyl, C<sub>1-8</sub>-alkylidene, C<sub>1-8</sub>-alkoxy, C<sub>1-8</sub>-heteroalkyl, C<sub>1-8</sub>-aminoalkyl, C<sub>1-8</sub>-haloalkyl, C<sub>1-8</sub>-alkoxycarbonyl, C<sub>1-8</sub>-hydroxyalkoxy, C<sub>1-8</sub>-hydroxyalkyl, or C<sub>1-8</sub>-alkylthio;~~

~~each R<sub>11</sub>, independently, is H, straight or branched chain C<sub>1-8</sub>-alkyl, C<sub>2-8</sub>-alkenyl, C<sub>2-8</sub>-alkynyl, C<sub>2-8</sub>-heteroalkyl, C<sub>2-8</sub>-aminoalkyl, C<sub>2-8</sub>-haloalkyl, C<sub>1-8</sub>-alkoxycarbonyl, C<sub>2-8</sub>-hydroxyalkyl, C(O)-C<sub>5-6</sub>-aryl substituted with C<sub>1-3</sub>-alkyl or halo, C<sub>5-6</sub>-aryl, C<sub>5-6</sub>-heteroaryl, C<sub>5-6</sub>-cycloalkyl, C<sub>5-6</sub>-heterocycloalkyl, C(O)NR<sub>12</sub>R<sub>13</sub>, CR<sub>5</sub>R<sub>12</sub>R<sub>13</sub>, (CH<sub>2</sub>)<sub>t</sub>NR<sub>12</sub>R<sub>13</sub>, t is an integer from 2 to 8; and~~

~~each R<sub>12</sub> and R<sub>13</sub>, independently, is H, C<sub>1-6</sub>-alkyl, C<sub>2-6</sub>-cycloalkyl, C<sub>5-6</sub>-aryl, optionally substituted with halo or C<sub>1-6</sub>-alkyl; or C<sub>5-6</sub>-heteroaryl, optionally substituted with halo or C<sub>1-6</sub>-alkyl; or R<sub>12</sub> and R<sub>13</sub> together form a cyclic structure;~~

~~or a pharmaceutically acceptable salt, ester or prodrug thereof.~~

36. (ORIGINAL) The method of claim 35 wherein the cholinergic receptor is a muscarinic receptor.

37. (ORIGINAL) The method of claim 36 wherein the muscarinic receptor is of the m1 muscarinic receptor subtype.

38. (ORIGINAL) The method of claim 36 wherein the muscarinic receptor is of the m4 muscarinic receptor subtype.

39. (ORIGINAL) The method of claim 36 wherein the muscarinic receptor is in the central nervous system.

40. (ORIGINAL) The method of claim 36 wherein the muscarinic receptor is in the peripheral nervous system.

41. (ORIGINAL) The method of claim 36 wherein the muscarinic receptor is in the gastrointestinal system, heart, endocrine glands, or lungs.

42. (ORIGINAL) The method of claim 36 wherein the muscarinic receptor is truncated, mutated, or modified.

43. (ORIGINAL) The method of claim 35 wherein the activity is a signaling activity of a cholinergic receptor.

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44. (ORIGINAL) The method of claim 35 wherein the activity is associated with muscarinic receptor activation.

45. (ORIGINAL) The method of claim 35 wherein the compound is a cholinergic agonist.

46. (ORIGINAL) The method of claim 35 wherein the compound is selective for the m1, or m4 muscarinic receptor subtype, or both the m1 and m4 muscarinic receptor subtypes.

47. (ORIGINAL) A method of activating a cholinergic receptor comprising contacting the cholinergic receptor or a system containing the cholinergic receptor with an effective amount of at least one compound of claim 1.

48 - 55. (CANCELED)

56. (CURRENTLY AMENDED) A method of treating a disease condition ~~associated with~~ caused by a cholinergic receptor comprising administering to a subject in need of such treatment an effective amount of at least one compound of claim 1.

57. (ORIGINAL) The method of claim 56 wherein the disease condition is selected from the group consisting of cognitive impairment, forgetfulness, confusion, memory loss, attentional deficits, deficits in visual perception, depression, pain, sleep disorders, psychosis, hallucinations, aggressiveness, paranoia, ~~and~~ increased intraocular pressure, neurodegenerative disease, Alzheimer's disease, Parkinson's disease, Huntington's chorea, Friederich's ataxia, Gilles de la Tourette's Syndrome, Down Syndrome, Pick disease, dementia, clinical depression, age-related cognitive decline, attention-deficit disorder, sudden infant death syndrome, and glaucoma.

58. (CANCELED)

59. (CURRENTLY AMENDED) The method of claim 56 wherein the disease condition is ~~associated with~~ caused by a cholinergic receptor dysfunction.

60. (CURRENTLY AMENDED) The method of claim 56 wherein the disease condition is ~~associated with~~ caused by decreased activity of a cholinergic receptor.

61. (CURRENTLY AMENDED) The method of claim 56 wherein the disease condition is ~~associated with~~ caused by loss of cholinergic receptors.

62 - 67. (CANCELED)

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68. (ORIGINAL) A method of treating a disease condition associated with reduced levels of acetylcholine comprising administering to a subject in need of such treatment an effective amount of at least one compound of claim 1.

69. (CURRENTLY AMENDED) A method of treating a condition selected from the group consisting of Alzheimer's Disease cognitive impairment, glaucoma, pain, and schizophrenia, comprising administering to a subject in need of such treatment an effective amount of at least one compound of claim 1.

70 – 73. (CANCELED)

74. (ORIGINAL) A method for identifying a genetic polymorphism predisposing a subject to being responsive to amount of at least one compound of claim 1, comprising:

administering to a subject an therapeutically effective amount of the compound;

measuring the response of said subject to said compound, thereby identifying a responsive subject having an ameliorated disease condition associated with a cholinergic receptor; and

identifying a genetic polymorphism in the responsive subject, wherein the genetic polymorphism predisposes a subject to being responsive to the compound.

75. (ORIGINAL) The method of claim 74 wherein the ameliorated disease condition is associated with the m1 or m4 muscarinic receptor subtype.

76. (ORIGINAL) A method for identifying a subject suitable for treatment with at least one compound of claim 1, comprising detecting the presence of a polymorphism in a subject wherein the polymorphism predisposes the subject to being responsive to said compound, and wherein the presence of the polymorphism indicates that the subject is suitable for treatment with said compound of claim 1.

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REMARKS

By present amendments, Applicants have incorporated into the specification a paragraph indicating that the present application is a divisional of a pending U.S. application, to which the present application claims priority. In addition, In this divisional application, Applicants are pursuing subject matter drawn to benzisoxazole and benzisothiazole compounds. Applicants have canceled the subject matter drawn to other unelected groups. Cancellation of the claims or the subject matter makes no admission as to the patentability thereof, and therefore, should not be so construed. Applicants reserve the right to pursue the canceled subject matter in this or any other continuation, divisional, or continuation-in-part application.

Applicants believe that the claims as presented herein are patentable and a notice to that effect is respectfully requested. No fee is believed due in connection with this preliminary amendment. However, if this is incorrect, the Director is hereby authorized to charge any necessary fees to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: Sept. 24, 2003

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